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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,696	01/19/2001	Daniel S. Sem	P-TB 4567	6467

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EXAMINER	
BAKER, MAURIE GARCIA	

ART UNIT	PAPER NUMBER
1627	14

DATE MAILED: 05/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/765,696	Sem
Examiner	**Art Unit**
Maurie Garcia Baker, Ph. D.	1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *THREE* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 5, 2002*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-9, 11-14, and 37* is/are pending in the applica

4a) Of the above, claim(s) *1-8* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *9, 11-14, and 37* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Response filed March 5, 2002 (Paper No. 12) is acknowledged. Claims 9, 11 and 12 were amended, claim 37 was added and claim 10 was cancelled. Therefore, claims 1-9, 11-14, and 37 are pending.

2. This application contains claims 1-8 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

3. Claims 9, 11-14 and newly added claim 37 are examined on the merits in this action.

4. It is noted with appreciation that the previous confusion with respect to the Information Disclosure Statement has been clarified by applicant (Response, page 10). Also, the Petition to Make Special that was never entered in the instant case will be forwarded to the correct office after the mailing of this Office Action. The examiner thanks applicant for resubmission of this document.

Withdrawn Objections/Rejections

5. The objection to the specification is withdrawn in view of applicant's amendments thereto. The rejections over Combs et al and He et al under 35 USC 102 are withdrawn in view

of applicant's amendments. The rejection of claim 11 under 35 U.S.C. 112, second paragraph is also withdrawn in view of applicant's amendments. The previous rejection under 35 USC 112, first paragraph for enablement is withdrawn in view of applicant's amendments; however, a new enablement rejection is set forth below based on the claims as amended. Additionally, a new rejection under 35 USC 103 (necessitated by amendment) is set forth below.

Maintained Rejections
Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 9, 11-14 and newly added claim 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a "method for identifying a population of bi-ligands". The claims use generic terminology such as "common ligand", "conserved site", "second ligand", "specificity site", "receptor family"

and "expansion linker". These terms are defined in the instant disclosure but the definitions are very broad.

The specification discloses **no** examples of the preparation and use of such "population of bi-ligands". These compounds are made up of pieces (i.e. "common ligand" and "second ligand") that could encompass very different moieties such as peptides and organic molecules. Additionally, the descriptions of "conserved site" as residues that are sufficient for activity (specification, pages 13-14) and "specificity site" as a binding site for a ligand exhibiting specificity for a receptor (specification, page 15) are simply not adequate support to show possession of the claimed invention. The disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

Response to Arguments

8. Applicant's arguments filed March 5, 2002 have been fully considered but they are not found persuasive. The examiner's rationale is set forth below.

9. Applicant argues the rejection by citing various portions of the specification's teachings (Response, pages 11-13). The examiner maintains that the teachings of the specification do not

adequately describe the claimed invention. This is discussed in more detail below. Also, in the Response, page 12, applicant disagrees with the examiner's assertion that there are no examples. The examiner was referring to specific working examples, not the general teachings referred to by applicant.

10. Note that "the essential goal of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." *In re Barker*, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978). Another objective is to put the public in possession of what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything that is in common use, or already known. *Evans v. Eaton*, 20 U.S. (7 Wheat.) 356 (1822).

11. While it is true that an example is not required, it is often necessary to provide description and enablement for broad claims (see paragraph 12 below). Thus, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38USPQ 189, 191 (CCPA 1938).

12. The examiner's position is that the disclosure does not provide adequate description of the claimed method. The examiner maintains that the art is unpredictable and the more unpredictable the art the greater the showing required (e.g. by "representative examples") for

both enablement and adequate disclosure. The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art.

13. Applicant argues that the newly amended claims are fully supported by the instant disclosure. The examiner respectfully disagrees. Although some of the terminology has been further defined in the claims (i.e. "common ligand" and "receptor"), description still is lacking for the "population of bi-ligands" for the reasons set forth in the rejection. Additionally, the descriptions of "specificity site" as a binding site for a ligand exhibiting specificity for a receptor (specification, page 15) are simply not adequate support to show possession of the claimed invention. The claim still describes the claimed method in *functional language* and the instant specification fails to identify that structure which is required for the claimed activity. Please see also paragraphs 17-23 below.

14. With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-

1175) regarding disclosure. For adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. Again, no working examples whatsoever have been provided in the instant case.

15. Lastly, an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). The examiner maintains because of the breadth of the claims, the unpredictability of the art and the lack of any working examples the above standard is not met. Thus the above rejection of claims 9, 11-14 and 37 under 35 U.S.C. 112, first paragraph is maintained.

New Rejections – Necessitated by Amendment
Claim Rejections - 35 USC § 112

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 9, 11-14 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method where the "receptor family" is a group of *one type* of enzymes (i.e. kinases) and the "common ligand" is a known cofactor to those enzymes or known mimic thereof, does not reasonably provide enablement for the claimed method using a "receptor family" made up of various enzymes where the "common ligand" is created based on unknown parameters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is clear from applicant's specification how one might practice this invention where the "receptor family" is a group of *one type* of enzymes (i.e. kinases) and the "common ligand" is a known cofactor to those enzymes or known mimic thereof; however, there is insufficient guidance as to how to make/use the claimed method using a "receptor family" made up of various enzymes where the "common ligand" is created based on unknown parameters. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;

(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: The claims are drawn to a "method for identifying a population of bi-ligands". No limitations on the specific structure of the "bi-ligand" are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention. For example, the "common ligand" and "second ligand" must bind to their respective sites and the sites must be able to be determined.

The state of the prior art and the level of predictability in the art: Compounds having two binding sites that bind to receptors such as kinases were known at the time of filing (see art rejections below); however, only limited numbers of such compounds were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of *any* such compound. Especially with respect to "cofactor binding site[s]", the prior art was only well established for known cofactors to single groups of enzymes or known mimics thereof. The "bi-ligands" of the instant claims require "common ligands" and a "second ligand"; however, such ligands were not generally known in the art for any and all such groups of enzymes. The structures of possible variants are sufficiently diverse and one of ordinary skill would not be able to predict their structures (and thus how to make such compounds) in the absence of any guidance without undue experimentation.

Applicant's claimed scope of compounds represents only an invitation to experiment regarding possible ligands and linkers of undefined structure.

Moreover, the claims require the presence of a "common ligand [that] binds to a cofactor binding site" and a "second ligand" to a "specificity site". One of ordinary skill would not know, *a priori*, how to determine such ligands for any receptor family and, most importantly, how to determine the cofactor binding site and specificity site since this is a very unpredictable area of the art. This is especially true since the cofactor binding site must be conserved across the receptor family. The instant specification fails to identify that structure which is required for the claimed activity.

It is noted that the claims now recite that the receptor is an enzyme and that the "common ligand binds to a cofactor binding site". However, the instant specification is deemed to not be enabling for determining a "cofactor binding site" for any group of seemingly unrelated enzymes. Again, the conserved site must be conserved across a receptor family and one of ordinary skill would not be able to determine such a site for seemingly unrelated enzymes without resorting to undue experimentation.

The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. Such persons of ordinary skill in this art, given its unpredictability, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

The existence of working examples and the quantity of experimentation needed to make or use the invention based on the content of the disclosure: Applicants have provided no working examples and the state of the prior art is such that one of ordinary skill could not

predict how to determine the "common ligand [that] binds to a cofactor binding site" for a receptor family made up of unrelated members, and further find a "second ligand" to a "specificity site" as required by the instant claims. The instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in making and using the claimed invention. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the invention would require undue experimentation.

Response to Amendment/Arguments

18. Applicant's arguments filed March 5, 2002 have been fully considered but they are moot in view of the new grounds of rejection set forth above. However, the following is noted.

19. The rejection under 35 USC 112, first paragraph for enablement has been rewritten as a scope of enablement rejection based on applicant's amendments. However, arguments and the declaration under 37 CFR 1.132 filed March 5, 2002 were not found persuasive to overcome this new rejection for the following reasons.

20. Applicant's declaration is confusing and does not appear to be directed to the invention as claimed. There are many steps in the method described in the declaration that simply do not appear to be recited in the instant claims. The declaration sets forth its methodology in terms that are not commensurate in scope with either the claims or the instant specification. For example, on page 2, paragraph 5 of the declaration, computational methods used to select common ligands are partially described, although no specific algorithm or parameters are set forth. Likewise, on page 2, paragraph 6, analogs of common ligands are made; and on page 3, paragraph 7, NMR experiments with "perturbations" are carried out. It is unclear how these experiments correlate with the limitations of the instant claims (and with the steps set forth in the instant specification).

21. Furthermore, Applicant's declaration recites various methods of making and using products that are ***not commensurate in scope*** with the instant claims. The declaration deals with very specific compound types. As stated above, the claims under examination recite no limitations on the specific structure of the "population" of "bi-ligands". Moreover, the instant declaration appears to be drawn to making and using a specific "bi-ligand library" not a "population" of "bi-ligands" (see declaration, page 4, paragraph 9).

22. See MPEP 2164.05: To overcome a prima facie case of lack of enablement, applicant must demonstrate by argument and/or evidence that the disclosure, as filed, would have enabled the claimed invention for one skilled in the art at the time of filing. This does not preclude

applicant from providing a declaration after the filing date which demonstrates that the claimed invention works. However, the examiner should carefully compare the steps, materials, and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e., that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. Such a showing also must be commensurate with the scope of the claimed invention, i.e., must bear a reasonable correlation to the scope of the claimed invention. In the instant case, the examiner deems that the declaration filed 3/5/02 does ***not*** bear reasonable correlation to the claimed scope.

23. Also see MPEP 716.09: Once the examiner has established a prima facie case of lack of enablement, the burden falls on the applicant to present persuasive arguments, supported by suitable proofs where necessary, that one skilled in the art would have been able to make and use the claimed invention using the disclosure as a guide. *In re Brandstadter*, 484 F.2d 1395, 179 USPQ 286 (CCPA 1973). Evidence to supplement a specification which on its face appears deficient under 35 U.S.C. 112 must establish that the information which must be read into the specification to make it complete would have been known to those of ordinary skill in the art. *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981). Affidavits or declarations presented to show that the disclosure of an application is sufficient to one skilled in the art are not acceptable to establish facts which the specification itself should recite. *In re Buchner*, 929 F.2d 660, 18 USPQ2d 1331 (Fed. Cir. 1991) (Expert described how he would construct elements necessary to the claimed invention whose construction was not described in the application or the prior art;

this was not sufficient to demonstrate that such construction was well-known to those of ordinary skill in the art.); *In re Smyth*, 189 F.2d 982, 90 USPQ 106 (CCPA 1951).

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. Claims 9, 11-14 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over He et al (On PTO-1449; Bioorg. Med. Chem. Lett., 1994, Vol. 4, No. 4, pp. 2845-2850).

The following interpretations are used for this rejection:

The specification defines a population as "a group of two or more different molecules" (page 14, line 4). He et al teach making two or more different molecules that comprise a common ligand (an ATP mimic) and a specificity ligand linked by a linker. As taught by the reference, these ligands can bind at least 2 different receptors from the same family (kinases) which bind ATP as a cofactor (reading on instant claims 11-12). The linker in the compounds of He et al is a simple methylene chain of variable length and as such would comprise a linker possessing perfect C2 symmetry as defined in the specification on page 10 (claims 13-14).

Specifically, He et al discuss the fact that kinases have two binding sites in the catalytic domain; one of these sites binds ATP while the other binds peptidic substrates (page 2845). He et al disclose making bisubstrate inhibitors "suitable to interact simultaneously with the ATP and the protein substrate binding domains" (page 2845, 2nd paragraph). The compounds contain an ATP mimic that would comprise the common ligand (that binds to a cofactor binding site) stated in the instant claims since this is a known "natural common ligand" for kinases (see specification, page 8-9). These compounds are of the general structure shown in Figure 2, with specific examples in Table 1. This ligand (ATP mimic) plus the methylene chain linker read on the claimed "module", with the different second ligands of He reading on the "second ligand" of the instant claims. He et al teach second ligands that are either an amine or an amino acid. The second ligand creates differences in the binding of the compounds with two different kinases, protein kinase C and c-AMP dependent protein kinase, as shown in Table 1. Changes in this second ligand are made due to differences in the binding sites of the *two different kinases* (page 2849), reading on different receptors in the "receptor family" of kinases.

He et al lack the specific teaching of identifying ligands that have specificity for a second and/or third receptor in the receptor family.

However, the instant claims would be obvious to one of ordinary skill in view of the teachings of He et al based on the fact that optimization of process steps, especially with respect to ordering, is within the routine skill of the art. *In re Burhans*, 154 F.2d

690, 69 USPQ330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results). Also, "[w]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA1955). With respect to the repetition of steps, see *In re Harza*, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to perform the method of He et al to identify ligands that have specificity for a second and/or third receptor in the receptor family. The general conditions of identifying bisubstrate inhibitors "suitable to interact simultaneously with the ATP and the protein substrate binding domains" of kinases was well-known as taught by He et al. One of ordinary skill would have been motivated to create different bisubstrate inhibitors because the similarity between the structures and properties is sufficiently close that one of ordinary skill would have been motivated to make additional inhibitors in searching for more potent compounds. One of ordinary skill would also have had a reasonable expectation of success based on the fact that He et al teaches the synthesis of such inhibitors.

Status of Claims/ Conclusion

26. No claims are allowed.

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday and alternate Fridays from 8:30 to 6:00.

29. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of

a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DR. JYOTHSNA VENKAT PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Maurie Garcia Baker, Ph.D.
May 17, 2002